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| 09/618,129      | 07/17/2000  | Xiao Bing Wang       | 55861-00003         | 8510             |

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EXAMINER

SPIEGLER, ALEXANDER H

ART UNIT

PAPER NUMBER

1637

DATE MAILED: 05/08/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

09/618,129

Applicant(s)

WANG, XIAO BING

Examiner

SPIEGLER

Art Unit

1637

-- The MAILING DATE of this communication appears on the cover sheet with the corresponding address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 13 February 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 2-38 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 2-38 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

  
**SHARON N. THORNTON**  
PATENT ANALYST

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.  
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All b) ☐ Some \* c) ☐ None of:  
1. ☐ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
\* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).  
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

## Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_ 6) ☐ Other:

### DETAILED ACTION

1. This action is in response to Paper No. 11, filed on January 22<sup>nd</sup>, 2002. Currently, claims 2-38 are pending. All arguments have been full considered and thoroughly reviewed, but are deemed not persuasive for the reasons which follow. This action is made FINAL. Any objections and rejections not reiterated below are hereby withdrawn.

THE FOLLOWING ARE NEW GROUNDS OF REJECTION NECESSITATED BY  
APPLICANTS AMENDMENTS TO THE CLAIMS

#### *Claim Rejections - 35 USC § 112*

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 2-38 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claims 2-38 are indefinite over “wherein the target nucleotide base in original form is not immediately adjacent on its 3’ side to an identical base”. (i.e. what is meant by original form? Does this mean two identical bases cannot be adjacent to each other?).

B) Claims 2-38 are indefinite over “the mutated base” because this lacks antecedent basis.

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

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5. Claims 2-38 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Applicants assert that support for claims 37-38 can be found on pages 4 and 18, however, pages 4 and 18 do not recite, "wherein the target nucleotide base in original form is not immediately adjacent on its 3' side to an identical base". Applicants should point to the specific page and line number to where there is support for newly added claims 37 and 38.

***Claim Rejections - 35 USC § 102***

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 2-15 and 23-38 are rejected under 35 U.S.C. 102(b) as being anticipated by Applied Genetics (WO 96/30545).

Applied Genetics teaches a method of detecting a target nucleic acid performing a primer extension reaction in the presence of three non-terminators (abstract, pgs. 16 and 58, Table 1A and B). The mutation can be any variant (pg. 14), the terminator is a dideoxynucleotide (pg. 6), the non-terminators and terminators may be labeled (pgs. 12-13).

*Claim Rejections - 35 USC § 103*

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

9. Claims 16-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Applied Genetics (WO 96/30545), as applied to claims 2-15 and 23-38 above, and in further view of Shuber (US 5,888,778).

The teachings of Applied Genetics are presented above. Specifically, Applied Genetics teaches a method of detecting a target nucleic acid performing a primer extension reaction in the presence of three non-terminators (abstract, pgs. 16 and 58, Table 1A and B).

Applied Genetics fails to teach the method wherein the primer is immobilized on a solid phase.

Shuber teaches that nucleic acids (i.e. a primer) can be bound to solid-phase supports (col. 4, ln. 25-26). Shuber teaches that the immobilization of nucleic acids are advantageous for simultaneously processing and screening a large number of samples and controls, and thus facilitating analysis, and furthermore, solid-phase supports can be used in automated systems.

In view of the teachings of Shuber, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Applied Genetics so as to have immobilized a primer on a solid-phase, instead of carrying out the method in solution, in

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order to have achieved the benefits of using solid-phase supports as taught by Shuber of simultaneously processing and screening a large number of samples and controls, and thus facilitating analysis, and furthermore, that solid-phase supports can be used in automated systems.

## **MAINTAINED REJECTIONS**

### ***Claim Rejections - 35 USC § 102***

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

11. Claims 2-38 are rejected under 35 U.S.C. 102(e) as being anticipated by Soderlund (US 6,013,431).

Soderlund teaches a method for detecting a target nucleic acid comprising:

- (a) providing a detectable amount of a target nucleic acid polymer in a single stranded form,
- (b) hybridizing the detectable amount of the nucleic acid polymer with one or more oligonucleotide primers (forming a primer-nucleic acid duplex), wherein each primer has a nucleotide sequence that is complementary to a sequence in the target nucleic acid polymer, such that when the primer is hybridized to the target nucleic acid polymer, the 3' end of the primer binds to a nucleotide flanking the specific nucleotide at the defined site in the target nucleic acid (i.e. the first unpaired base immediately downstream of the 3' end of the primer), (c) exposing

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the hybridized nucleic acid polymer to a polymerization agent in a mixture containing at least one deoxynucleotide, said deoxynucleotide comprising a detectable label, and one or more chain terminating nucleotide analogues, such that a detectable primer extension product is formed if the labeled deoxynucleotide is complementary to the specific nucleotide at the defined site, and (d) analyzing the polymerization mixture of step (c) for the presence or absence of the primer extension product containing the labeled deoxynucleotide at the 3' end thereof, whereby the identity of the specific nucleotide at the defined site is determined (col. 18, ln. 19-53).

The reference also teaches that two or more differently labeled dNTPs (non-terminator nucleotides) can be added to the primer-nucleic acid duplex, wherein the detection is better interpreted by adding dNTPs that are different than the terminator nucleotide (col. 8, ln. 58-64). The reference also teaches the use of this invention with various labels such as radioactive or fluorescent labels (see examples 1-7, col. 9-18). The reference also teaches that the primer extension reaction can be performed by enzymatic means using template dependent enzymes (i.e. T7 DNA polymerase, T4 DNA polymerase, reverse transcriptase, etc.) (col. 8, ln. 10-17). The reference also teaches that the primer may contain an attachment moiety (i.e. biotin, antigens, etc.) (col. 6, ln. 16-31), that permits affinity separation of the from the unincorporated reagent and/or the nucleic acid of interest (col. 6, ln. 53 to col. 7, ln. 26), and furthermore, that a solid support may be used in the separation process (col. 6-7). The reference also teaches that the nucleic acid of interest can be any human, animal, plant, or microbe (col. 5, ln. 25-32).

*Applicants Arguments*

12. Applicant argues that Soderlund fails to disclose or suggest incorporating multiple types and a plurality of labeled nucleotides to the primer, as Soderlund's method terminates immediately after incorporation of the single labeled nucleotides complementary to the target nucleotide.

*Response to Applicants Arguments*

13. Applicants arguments fail to persuade, as Soderlund does teach a method that incorporated multiple types and a plurality of labeled nucleotides to the primer (i.e. one or more labeled deoxynucleotides (col. 18). Furthermore, Claims 37 and 38 are drawn to detection methods that rely on the detection of the presence of the detectable signal of the non-terminator nucleotides (i.e. deoxynucleotides), as does Soderlund (col. 18). Therefore, Applicants invention is not distinguishable over Soderlund.

*Conclusion*

14. No claims are allowable.

15. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37



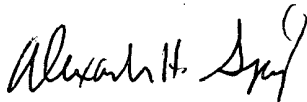
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CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

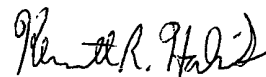
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alexander H. Spiegler whose telephone number is (703) 305-0806. The examiner can normally be reached on Monday through Friday, 7:00 AM to 3:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (703) 308-1119. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 and (703) 305-3014. Applicant is also invited to contact the TC 1600 Customer Service Hotline at (703) 308-0198.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.



Alexander H. Spiegler  
May 6, 2002

  
**KENNETH R. HORLICK, PH.D**  
**PRIMARY EXAMINER**

5/6/02